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|-----------------|-------------|----------------------|---------------------------|------------------|
| 09/891,445      | 06/26/2001  | Yunhua N. Jeng       | 11916.0048.NPUS00(MOPV048 | 6324             |

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EXAMINER

TELLER, ROY R

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 05/01/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/891,445

Applicant(s)

JENG ET AL.

Examiner

Roy Teller

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 3 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2 & 4-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This office action is in response to Paper No: 10, received 2/21/03, in which applicant cancelled claim 3 and amended claims 1, 9, 14, 18, and 19.

Claims 1-2 and 4-22 will be examined.

#### ***Claim Rejections - 35 USC § 112***

The rejection of claims 9, 14, 18, and 19 under 35 USC 112, second paragraph, is withdrawn pursuant to applicant's arguments, which were persuasive.

The rejection of claim 18 under 35 USC 112, first paragraph, is withdrawn pursuant to applicant's arguments, which were persuasive.

#### ***Claim Rejections - 35 USC § 102***

The rejection of claims 1, 5, 10, 14, 15, and 18-20 under 35 USC 102(b) is withdrawn pursuant to applicant's arguments, which were persuasive.

#### ***Claim Rejections - 35 USC § 103***

The rejection of claims 1-2 and 4-22 under 35 USC 103(a) is withdrawn pursuant to applicant's arguments, which were persuasive.

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## **New Rejections**

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4, 5, and 8-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magruder (USPN 5,037,420) in view of Mitchell (USPN 5,474,980).

The claimed invention is drawn to a composition of matter comprising human, equine, bovine or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or an oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier. Dependent claims recite the first BEC present from about 0.1% to about 10% by weight of the composition and the second BEC from about 1% to about 20% by weight of the composition. The first BEC comprises a non-ionic surfactant. The second BEC contains a selection of oxo-acid salts.

Magruder teaches porcine, bovine, equine, and human growth promoting hormone, column 13, lines 66-68 and column 14, line 1. Magruder discloses somatotropin in column 14, line 11. Margurder also teaches a pharmaceutical carrier composed of the agent, a buffer and a surfactant, column 14, lines 39-40. Magruder's buffer can comprise sodium phosphate

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monobasic or sodium phosphate dibasic from 20% to 45% , column 15, lines 36-37. Magruder discloses non-ionic surfactants such as polyoxyethylene sorbitan monooleate, polyoxyethylene stearate and Tween 80, from 0.001% to 7.5%, column 15, lines 58-59, 61-62, and 68.

Magruder does not teach a non-aqueous carrier or a fluidly injectable composition.

Mitchell teaches a composition of somatotropin comprising a biocompatible oil, sesame oil, which constitutes a predominate part by weight of a composition , column 6, lines 27 and 35-36 together with aluminum monostearate as an antihydration agent, comprising between 1% to 10% by weight, column 7, lines 36-37 and lines 44-45. Mitchell teaches that the oil and monostearate are useful for prolonged parental release of the somatotropin (see the abstract). Mitchell teaches somatotropin with preferred polyvalent metals such as zinc, column 4, lines 51-52. Mitchell discloses that oils that are liquid at about 25C may facilitate injection of some compositions of the invention, see column 6, lines 13-14. Mitchell teaches an injectable substantially nonaqueous suspension, see claim 1, column 19.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have formulated the composition disclosed by Magruder in the biocompatible oil/ aluminum monostearate vehicles taught by Mitchell because Mitchell teaches that the oil/ monostearate vehicles are useful for prolonged parental release of somatotropin *in vivo*.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Magruder in view of Mitchell, as applied to claims 1, 14 and 18 above, and further in view of Scarborough (USPN 6,162,258).

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The claimed invention is drawn to a composition of matter comprising human, equine, bovine or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or an oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier. Dependent claims recite non-ionic surfactants as selected from: polyoxyethylene fatty acids esters, poloxamers, polyoxyethylene sorbitan fatty acid esters, tocopherol polyethylene glycol succinates, sugar fatty acid esters, polyoxyethylene glycerides, and polyoxyethylene vegetable oils.

While Magruder discloses a biological implant but does not mention the temperature of the implant, absent some evidence to the contrary, the implant would be implanted in an animal (approximately 37-39C).

Magruder in view of Mitchell, teach a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra*. Magruder in view of Mitchell does not teach the aforementioned non-ionic surfactants.

Scarborough teaches a polyoxyethylene sorbitan fatty acid ester and a polyoxyethylene fatty acid ester mixed with a growth hormone such as somatotropin, column 5, lines 1-2 and 5, column 6, lines 48-49.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the non-ionic surfactants of Scarborough to the composition disclosed by Magruder in view of Mitchell in order to enhance the bioavailability of

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somatotropin in the composition, because Scarborough teaches biocompatibility in the healing response, column 3, lines 55 and 61.

Claims 6 and 7 are rejected under 103(a) as being unpatentable over Magruder in view of Mitchell, as applied to claims 1, 14 and 18 above, and further in view of Hamilton (USPN 4,816,568).

The claimed invention is as described above, wherein the second BEC is a non-reducing carbohydrate selected from one polyol and one carbohydrate ester, which include: tehalose, sucrose, mannitol, sorbitol, trehalose octaacetate, trehalose dihydrate, sucrose octaacetate, and cellobiose octaacetate.

Magruder in view of Mitchell teach a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra*. Magruder in view of Mitchell do not teach the polyol or carbohydrate ester.

Hamilton teaches polyols selected from sucrose, mannitol, and sorbitol. The polyol can be present in amounts from about 2.5% to about 99% by weight of the total weight of the overall formulation, column 3, lines 64, 66-67, and column 4, lines 16-18.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the polyol stabilizer of Hamilton to the composition disclosed by Magruder in view of Mitchell in order to enhance the bioavailability of the somatotropin in the composition, because Hamilton teaches that growth hormones may be admixed with various stabilizers to provide for the preservation of the soluble bioactivity of the growth hormone, see abstract.

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*Conclusion*

All claims are rejected

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is (703) 305-4243. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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4/29/03

RT

*Brenda Brumback*  
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